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The usefulness of S100β protein and fractalkine in predicting traumatic brain injury in pediatric patients with minor head trauma

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ABSTRACT

Aims: In this study it was aimed to demonstrate the effectiveness of S100β protein levels which are biomarkers related to central nervous system, and fractalkine levels, which are known to play a role in inflammation processes in prediction trauma induced brain damage.

Methods: Patient aged 2 to 18 years who came to the emergency department due to minor head trauma and underwent brain computer tomography were included in our study. It was investigated whether there was a relationship between the two groups, according to the causes of trauma, symptoms at presentation and the level of serum S100β and Fractalkine according to the lesions detected in cranial computer tomography.

Results: The other symptoms including vomiting, retrograde amnesia, loss of consciousness, confusion, post traumatic amnesia is significantly higher in patients with brain lesions (p<0,05). Patients with lesions on cranial computer tomography have significantly low Glasgow coma score. (p<0,05). Patients with lesions on cranial computer tomography have a significantly high S100β and Fractalkine levels. (p<0,05). S100β area under the curve 0.700 sensivity is 55%, specificity is 87.5%. Fractalkine area under the curve 0,785, sensitivity is 62.5% specificity is 85%.

Conclusion: As a result, the child patients with cranial computer tomography lesions from minor cranial trauma levels for S100β and Fractalkine levels are significantly higher and can be a criteria for cranial computer tomography usage in emergency medicine.

Keywords: Child, fractalkinee, head trauma, S100β

INTRODUCTION

Trauma is one of the major causes of morbidity and mortality in childhood. In high-income countries, 691/100.000 children are taken to emergency departments due to head trauma (traumatic brain injury (TBI) every year.[1] It is considered as a public health problem since it is among the causes of preventable mortality and morbidity all over the world.[2]

While indoor falls are the most common cause of head trauma in children under 2 years of age, the frequency of motor vehicle accidents increases in play-age and school-age children and reaches similar rates with falls.[3]

Minor head trauma (MHT) constitutes 90% of all head traumas, and a small part leads to clinically significant TBI.[4] The use of brain computed tomography (BCT) is recommended for this purpose.[5] Children with MHT constitute 40-60% of all TBIs examined by BCT. Less than 10% of them show radiological signs of TBI.5 Approximately 1% of children who are considered to have mild TBI need neurosurgical intervention, and 0.2% of these cases die.[5,6]

It is estimated that the rate of fatal malignancy caused by pediatric BCT scans is between 1/1000-1/5000 and that there is a higher risk at younger ages.[7,8] Therefore, they attempted to develop algorithms for use in children with MHT. The Pediatric Emergency Care Applied Research Network (PECARN) algorithm is the most commonly used of these algorithms.[9]

Recently, the view that some serum markers (S100β protein and neuron-specific enolase (NSE), Tumor Necrosis Factor (TNF), Glial fibrillary acidic protein (GFAP), TNF-α, interleukin (IL)-6 and myelin basic protein (MBP) can be used to detect trauma-related damage in patients with MHT has rapidly become valuable and studies are shifting accordingly.[10,11]

The S100β protein is a member of the calcium-binding S100 protein family and is expressed from the subtype of mature astrocytes in the central nervous system and the Schwann cells in the peripheral nervous system. While the levels of S100β protein are quite low in normal people, there is an increase first in the cerebrospinal fluid (CSF) and then in blood levels in the presence of brain injury, which is due to the impaired blood brain barrier. In many studies, the increase in S100β protein blood levels has been found to be associated with abnormalities in BCT.[12]

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Fractalkine (FKN) is a glycoprotein and is an adhesion molecule for monocytes, T cells and natural killer cells. It has been demonstrated in studies that FKN is involved in many inflammatory processes such as coronary artery disease, asthma, and rheumatoid arthritis.[13]

In this study, it was aimed to reveal the effectiveness of the levels of S100β protein, one of the biomarkers related to the central nervous system, and the levels of fractalkine, which is known to be involved in inflammation processes, in predicting brain injury due to trauma.

METHODS

Our study was conducted prospectively in Kahramanmaraş Sütçü İmam University, Department of Emergency Medicine with the ethics committee approval dated 21.09.2021 and numbered 2021/31 of Kahramanmaraş Sütçü İmam University Non-interventional Clinical Researches Ethics Committee (GAEK). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Age, gender, causes and symptoms of trauma, lesions detected in BCT, serum S100β and serum FKN levels of the patients included in the study were examined.

In our study, patients who underwent BCT according were divided into two groups as those with and without lesions. Among the patients with lesions, 40 patients who met the exclusion criteria were randomly selected. Among the patients without lesions, 40 patients who met the exclusion criteria were randomly selected.

Statistical Analysis

The data obtained in our study were recorded and analyzed in the IBM SPSS Statistics 21 program. The normality of the data was tested by the Kolmogorov-Smirnov test. Median and interquartile range (IQR) were used to represent non-parametric data, and the number of cases (n) and percentile (%) were used to represent the categorical variables. The Mann-Whitney U test was used to compare non-parametric data with categorical variables, the Pearson Chi-square test was used for the analysis of categorical variables within themselves, and the Spearman correlation test was used to compare non-parametric variables within themselves. The ROC curve was used to calculate the area under the curve (AUC), cut-off value, specificity and sensitivity of the data. A value of $p<0.05$ was considered significant for all tests.

RESULTS

In our study, the S100β level of the patients with lesions on BCT was 11.1 pg/mL (IQR: 126.9 pg/mL), and the S100β level of the patients without lesions was 0 pg/mL (IQR: 0.1 pg/mL). S100B levels of patients with lesions were found to be significantly higher ($p<0.05$) (**Figure 1**).

In our study, the FKN level of the patients with lesions on BCT was 546.2 pg/mL (IQR: 447.4 pg/mL), and the FKN level of the patients without lesions was 293.3 pg/mL (IQR: 235.9 pg/mL). The FKN level of the patients with lesions were found to be significantly higher ($p<0.05$) (**Figure 2**).

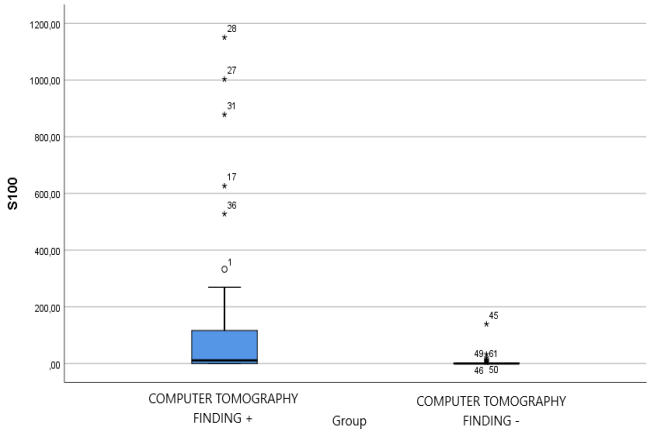

Figure 1. Relationship between the presence of trauma and the level of S100β (p:0.001)

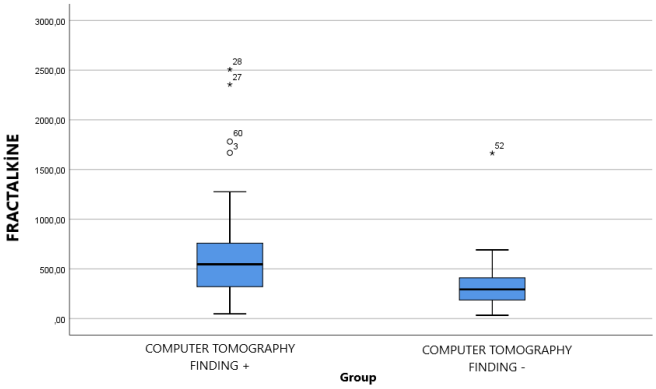

Figure 2. Relationship between the presence of trauma and the level of S100B (p:0.000)

Relationship of GCS with S100β and fractalkine levels at **Table 1**.

Table 1. Relationship of GCS with S100β and fractalkine levels

	Glasgow Coma Score (GCS)		
	15 (n:75) Median (IQR)	14 (n:5) Median (IQR)	P
S100β	0 (14.5)	94.5 (571.7)	0.047
Fractalkine	360.7 (346.9)	621.5 (455.1)	0.088

In our study, the level of S100B was found to be significantly higher in patients with EDH, SDH, depressed fracture and contusion ($p<0.05$). The S100β levels of the patients with SAH, linear fracture and subgaleal hematoma were similar to those without them ($p>0.05$) (**Table 2**).

Table 2. Relationship between the lesions detected on BCT and the S100β level

	Lesion + S100β Median (IQR)	Lesion - S100β Median (IQR)	p
Epidural hematoma	70.7 (614.9)	0 (12.1)	<0.001
Subdural hematoma	250.9 (528.0)	0 (10.3)	<0.001
Subarachnoid hemorrhage	0	0 (33.4)	0.365
Linear fracture	0 (82.1)	0 (14.4)	0.302
Depressed fracture	75.1 (461.3)	0 (11.4)	0.006
Subgaleal hematoma	0 (194.4)	0 (16.0)	0.635
Contusion	34.8 (300.7)	0 (11.4)	0.024

In our study, the level of FKN was found to be significantly higher in patients with EDH, SDH and linear fracture ($p<0.05$). The FKN levels of the patients with SAH, depressed fracture, subgaleal hematoma and contusion were similar to those without them ($p>0.05$) (**Table 3**).

Table 3. Relationship between the lesions detected on BCT and the level of fractalkine

	Lesion + Fractalkine Median (IQR)	Lesion - S100β Median (IQR)	p
Epidural hematoma	674.6 (257.8)	344.6 (329.3)	0.002
Subdural hematoma	714.4 (672.9)	342.1 (339.7)	0.002
Subarachnoid hemorrhage	494.8	363.5 (374.8)	0.628
Linear fracture	568.8 (432.6)	363.5 (288.1)	0.004
Depressed fracture	464.5 (1295.8)	362.0 (380.2)	0.217
Subgaleal hematoma	570.1 (785.8)	348.4 (310.5)	0.097
Contusion	587.4 (759.4)	344.6 (338.8)	0.053

In our study, for the presence of lesions on BCT, the AUC value of S100β was 0.700 (95Cl: 0.583-0.817), the appropriate cut-off value was 8.7, and the sensitivity and specificity at this value were found to be 55% and 87.5%, respectively. In our study, for the presence of lesions on BCT, the AUC value of FKN was 0.748 (95Cl:0.638-0.858), the appropriate cut-off value was 456.0, and the sensitivity and specificity at this value were found to be 62.5% and 85, respectively (**Figure 3**).

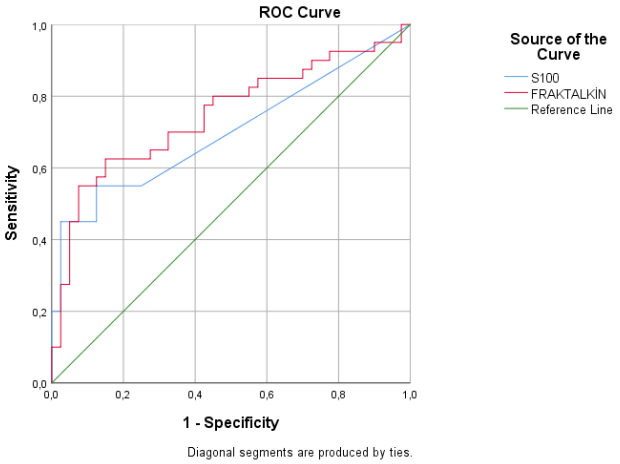

Figure 3. ROC analysis of S100β and fractalkine levels for the presence of lesions on BCT

DISCUSSION

The biomarkers of brain injury are promising for facilitating early management and triage decisions.[14] Furthermore, the development of biomarkers in MHT is important since it will reduce unnecessary requests for BCT and therefore exposure to radiation in childhood.[15] In a study, it was indicated that the rate of BCT scan decreased by 34% with the use of S100β.[16]

While there some potential markers of brain tissue fate, S100β is the most studied protein biomarker of brain injury.15 In the study of Piazza, the level of S100β was found to be high in children with MHT.[17] Filippidis et al.[18] indicated that some authors may have made a biased selection according to the BCT finding in cases with mild head trauma, however, studies on S100β were promising.In our study, it was determined that the S100β level of patients with positive intracranial lesion among patients with MHT was significantly higher.

In the study conducted by Zanier et al.[19] in mice induced with traumatic brain injury, they stated that although there was a temporary protection of brain tissue in the early stages of TBI in the absence of FKN, there was a deterioration in the late period. In an experimental study, it was demonstrated that the fractalkine level of the subjects with mild trauma increased significantly at the 8th hour and played a role in the activation of the immune system.[20] In our study, it was determined that the level of FKN was significantly increased in patients with intracranial lesions. In our study, the presence of lesions on BCT was found to be significantly higher in cases brought due to falling from high. Although S100β and FKN levels were found to be high in ADTK, this relationship was not statistically significant. This situation can be explained by the increase in the incidence of intracranial lesion as a result of the high severity of trauma in ADTK and in cases of falling from high, and thus the increase in S100β and FKN levels.

In a meta-analysis, it was reported that there was a significant relationship between S100β and GCS.[16] In our study, 93.7% and 6.3% of the patients had a GCS of 15 points and 14 points, respectively, BCT finding positivity and S100β level were found to be significantly higher in patients with a GCS of 14, and although the FKN levels of the patients with a GCS of 14 were found to be high, it was not statistically significant.

In their review, Thelin et al.[15] indicated that S100β was sensitive enough to detect and evaluate different traumatic intracranial lesions such as cerebral contusions, SDHs, traumatic SAH and EDH.In our study, while S100β level and FKN were found to be significantly higher in EDH and SDH, S100β was significantly higher in patients with depressed fracture and contusion, and the level of FKN was significantly higher in patients with linear fractures. S100β and FKN levels of SAH and subgaleal hematoma were similar in patients with and without intracranial lesion.

In a study, when BCT findings were used as a factor to evaluate S100β marker performance, it was reported that the sensitivity was 100%, the specificity was 42%, and the AUC was 0.68.[20] No study evaluating the sensitivity and specificity of FKN level was found in the literature. In our study, the AUC of S100β was 0.7, the sensitivity was 55%, and the specificity was 87.5% for the presence of lesions on BCT, and AUC was 0.748, the sensitivity was 62.5%, and the specificity was 85% for FKN. Considering these values, we think that we can say that both S100β and FKN support the presence of lesions on BCT.

In our study, the S100β and FKN levels of the patients with lesions on BCT were found to be significantly higher. S100β and FKN levels were found to be significantly higher in patients with retrograde amnesia and loss of consciousness. In our study, although the FKN levels of patients with a GCS of 14 were found to be high, they were not statistically significant. While the S100β level and FKN level were found to be significantly higher in EDH and SDH, the S100β level was significantly higher in patients with depressed fracture and contusion, and the FKN level was significantly higher in patients with linear fractures. S100β and FKN levels of SAH and subgaleal hematoma were similar in patients with and without intracranial lesions. AUC was 0.700, sensitivity was 55% and specificity was 87.5% for S100β, and AUC was 0.748, sensitivity was 62.5%, and specificity was 85% for FKN.

CONCLUSION

In pediatric patients presenting with MHT, the S100β and FKN levels were found to be high in patients with BCT lesions, which causes a view that it can be included in BCT scan criteria. Nevertheless, there is a need for more studies especially in terms of FKN.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Kahramanmaraş Sütçü İmam University Non-interventional Clinical Researches Ethics Committee (GAEK) (Date: 21.09.2021, Decision No: 2021/31-9).

Informed Consent: All patients signed and free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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